REMARKS

Claim Amendments

Claims 1-1, 5-18, 22-28, and 38-45 are pending in the application. Claims 1, 2, 5-14, 16-18, 22-24, 28-29, 32-34 have been amended. Claims 3, 4, and 19-21 have been cancelled. Claims 38-45 have been added.

Support for claim 38 can be found, for example, at page 7, lines 26-29. Support for claim 39 can be found, for example, at page 8, lines 13-15. Support for claim 40 can be found, for example, at page 14, lines 2-5. Support for claim 41 can be found, for example, at page 7, lines 25-29. Support for claim 42 can be found, for example, at page 8, lines 19-21. Support for claim 43 can be found, for example, at page 6, lines 23-26. Support for claim 44 can be found, for example, at page 5, lines 1-14. Support for claim 45 can be found, for example, at page 13, lines 20-23.

No new matter has been added. Reconsideration and reexamination are respectfully requested in view of the amendments and the following remarks.

Withdrawn Claims

The Examiner indicated that claims 29-37, added in response to the Examiner's previous restriction requirement, are required to be withdrawn from consideration as being directed to a non-elected invention. The applicants respectfully request reconsideration and withdrawal of this requirement in accordance with 37 CFR § 1.143.

Applicants admit that the inventions of claims 29-37 are obvious over the inventions of claims 1-2, 5-18, 22-28, and 38-45, and vice versa. Therefore, restriction should not be required. The Examiner's attention is directed to MPEP § 803.

The Examiner argues that the invention of claims 29-37 is independent or distinct from the invention in the elected and pending method claims because it "can be used for different processes, such as analysis of other peptide or other biological samples." However, the pending method claims are also applicable to the analysis peptides of proteins (see, e.g., Specification page 10, line 28-31; page 13, lines 1-10). In addition, the proteins for the pending method claims

are equally obtainable from a variety of types of biological samples (see, e.g., Specification page 9, line 26 to page 10, line 8). Thus, both the method claims and the system of claims 29-37 are equally usable for "other peptides or other biological samples".

For all of the above reasons, the applicants respectfully submit that claims 29-37 should not be withdrawn and should be considered in conjunction with the pending method claims. Accordingly, the applicants request that the Examiner not withdraw claims 29-37. The applicants also request that claims 29-37 be considered in their current version.

Claim Rejections 35 U.S.C. § 103

The Examiner rejected claims 1-18 and 22-28 under 35 U.S.C. § 103 as allegedly obvious over any of five references: U.S. Patents Nos. 5,869,240 or 5,827,659 ("Patterson"), U.S. Patent No. 4,507,555 ("Chang"), Wang et al., Abstract, Combinatorial Chemistry and High Throughput Screening 2(6):327, 1999 ("Wang"), or Demirev et al., Abstract, Analytical Chemistry 69(15):2893, 1997 ("Demirev"). The applicants respectfully disagree.

The applicants' invention provides methods and systems for the analysis of proteins taken from a biological system at multiple time intervals. In the pending method claims, including independent claims 1 and 22, each of the multiple samples is separated into multiple protein samples, and the multiple protein samples are then analyzed using a parallel array of mass spectrometers. The mass spectrometers generate mass spectral data indicating identity and abundance of proteins. The system claims, including independent claim 29, provide a system for such methods. In all of the claims, a common computing device collates the mass spectral data as a function of the time of sampling of the biological system.

The applicants' invention is useful for the analysis of temporal changes in the expression of proteins in a biological system – i.e. for time-resolved proteomic analysis. To this end, the invention is capable of efficiently analyzing large numbers of proteins while producing data that is meaningfully expressed as a function of time. (See, e.g., Specification page 8, lines 10-29; page 5, lines 1-2, 15-17, 23-25; page 7, lines 25-26.)

The applicants respectfully submit that none of the references cited by the Examiner, either alone or in combination, describe or suggest the methods of claim 1 or 22, or the system of claim 29. In particular, none of the references teaches sampling a biological system at multiple time intervals, let alone collating mass spectral data from a parallel array of mass spectrometry systems based on time of sampling. Because none of the references teaches or suggests collating mass spectral data from a parallel array of mass spectrometry systems for multiple proteins sampled at multiple times, the applicants respectfully submit that all of the claims are allowable.

The Patterson reference, for example, describes methods and apparatus for sequencing polymers, such as peptides, using mass spectrometry. The polymers are hydrolyzed or otherwise digested to create a series of overlapping fragments, which are analyzed by a mass spectrometer. The resulting mass data for the overlapping fragments, i.e. the "parallel" mass spectra, are then analyzed to determine the sequence of monomers in the polymer. Patterson describes particular methods for digesting the polymers and for evaluating their mass spectra to ascertain the sequence of monomers.

Patterson does not, however, describe or suggest multiple samples of a biological system taken at multiple times, or collating of mass spectral data as a function of the time of sampling of the biological system, as required by claims 1, 22, and 29. Patterson also does not describe or suggest a parallel array of mass spectrometers, as required by claims 1, 22, and 29; rather, Patterson describes "parallel" spectra for the various overlapping polymer fragments. For any of these reasons, the applicants respectfully submit that none of claims 1, 22, and 29 is rendered obvious by one or both of the Patterson references, alone or in combination with any of the other cited references. Accordingly, claims 1, 22, and 29 are allowable over Patterson.

The Chang reference describes a system for separate but synchronized mass spectral analyses of a single sample. The system is referred to as a parallel mass spectrometer (PMS) because it has two or more sets of ion extraction means, mass resolution devices, and ion detectors that are connected in parallel rather than in tandem. Importantly, in the Chang system, a single gas chromatogram receives a single sample (see, e.g., Chang Fig. 1). By conducting different analyses of the sample at the same time, the system can synchronize outputs such as a

SIM chromatogram and a mass spectrum, thereby negating the need to reconstruct the former from the latter and simplifying the overall analysis of the sample.

Chang also does not, however, describe or suggest the analysis of multiple samples of a biological system taken at multiple times, or collating of mass spectral data as a function of the time of sampling of the biological system, as required by claims 1, 22, and 29. Neither does Chang describe or suggest a parallel array of mass spectrometry systems that receives multiple protein samples, as required by claims 1, 22, and 29; rather, Chang describes a system for doing multiple analyses of a single sample. For any of these reasons, the applicants respectfully submit that none of claims 1, 22, and 29 is rendered obvious by Chang, alone or in combination with any of the other cited references. Accordingly, claims 1, 22, and 29 are allowable over Chang.

The Wang reference, in contrast to Chang, describes a parallel spray interface for use with multiple chromatography columns and a single mass spectrometer. The interface allows the flow from the columns to be sampled rapidly and sequentially or, as described in a previously reported interface, simultaneously. Thus, samples from each of the multiple columns can be taken and analyzed by the single mass spectrometer while elutions from the columns continue.

But like Patterson and Chang, Wang does not describe or suggest the analysis of multiple samples of a biological system taken at multiple times, or collating of mass spectral data as a function of the time of sampling of the biological system, as required by claims 1, 22, and 29; rather, Wang describes a system for collecting components of separations while the separation proceeds. In addition, Wang clearly does not describe or suggest a parallel array of mass spectrometers as required by claims 1, 22, and 29. For any of these reasons, the applicants respectfully submit that none of claims 1, 22, and 29 is rendered obvious by Wang, alone or in combination with any of the other cited references. Accordingly, claims 1, 22, and 29 are allowable over Wang.

Demirev appears to describe methods for the analysis of mass spectral data such as might be obtained for short peptides in a library of peptides. Demirev notes a variety of statistics that are calculated in order to characterize a set of computer-generated data and evaluate the prospects for analysis of real data. However, Demirev does not describe any method or system,

theoretical or actual, for the production of such mass distributions. Thus, Demirev does not describe or suggest the analysis of multiple samples of a biological system taken at multiple times, or collating of mass spectral data as a function of the time of sampling of the biological system, as required by claims 1, 22, and 29. Neither does Demirev describe or suggest a parallel array of mass spectrometers as required by claims 1, 22, and 29. For any of these reasons, the applicants respectfully submit that none of claims 1, 22, and 29 is rendered obvious by Demirev, alone or in combination with any of the other cited references. Accordingly, claims 1, 22, and 29 are allowable over Demirev.

For any and all of these reasons, the applicants respectfully submit that claims 1, 22, and 29 are allowable. Claims 2, 5-18, and 38-45 depend from claim 1, and are allowable at least for any of the reasons given for claim 1. Claims 23-28 depend from claim 22, and are allowable at least for any of the reasons given for claim 22. Claims 30-37 depend from claim 29 and are allowable at least for any of the reasons given for claim 29. Accordingly, claims 2, 5-18, 23-28, 30-37, and 38-45 are also allowable.

In summary, the applicants respectfully request reconsideration of the Examiner's withdrawal of claims 29-37 and rejection of claims 1-18 and 22-28. Allowance of claims 1-2, 5-18, and 22-45 is earnestly solicited.

Enclosed is a check including the amount of $420.00 for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

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